IPAC-RS
International Pharmaceutical Aerosol Consortium on Regulation & Science

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By Email: hc.policy.bureau.enquiries.sc@canada.ca

Bureau of Policy, Science and International Programs
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Re: Draft Guidance Document for Consultation: Comparative Pharmacokinetic Studies for Orally Inhaled Products[1,2]

Dear Health Canada,

Members of the International Pharmaceutical Aerosol Consortium on Regulation & Science (IPAC-RS) appreciate the issuance of the draft guidance "Comparative Pharmacokinetics Studies for Orally Inhaled Products" and would like to offer the following comments for your consideration. IPAC-RS is a non-profit association of companies that develop, manufacture, or market orally inhaled and nasal drug products – both brand-name and generic. The list of current full and associate IPAC-RS members is at https://ipacrs.org/about/list-of-member-companies/.

IPAC-RS recognizes the challenges of establishing bioequivalence of orally inhaled products, which have numerous factors that may influence their performance, such as formulation-related factors (e.g., single actuation content and aerodynamic particle size distribution), the delivery device, and patient-related factors.

IPAC-RS commends Health Canada's efforts to provide public guidance reflecting the Agency's current thinking, and would welcome opportunities for further discussion of these topics.

Line	*Original Language*	*Proposed Changes*	*Justification of Proposed Change*
Line 79-81	*This guidance also applies when a significant change is made to a reference product, such that a comparative clinical trial would previously have been required in support of the change*	"This guidance also applies when a significant change is made to **the original developed/submitted product**, such that a comparative clinical trial would previously have been required in support of the change".	Terminology used – the term 'reference product' is used in development of generic products to indicate the originator (brand-name) and thus 'reference' for generic products to be developed against. In this context, we do not believe this is the intention of the text and perhaps it is better to change the terminology to 'original developed/submitted product'.
Line 103	*For those products where in vivo comparative pharmacokinetic studies are not appropriate*		This is vague and open to interpretation (meaning that a regulatory meeting is likely) whereas the 2018 recommendations (line 112) are clearer – please utilize the wording from that document to aid clarification.
Line 105			Citing the steroid guidance without specific examples adds confusion. Recommendation: This paragraph is the crux of the entire guidance and it needs to be clearer so the user can distinguish when PK is sufficient and when PD is needed. Please add clarification and specific examples.
Lines 153-158			It would be helpful if a more quantitative measure of "significant gastrointestinal absorption" was provided, as conducting studies with and without charcoal block would add to the complexity of the clinical study.
Lines 168-169	*The selected sampling times should be justified and specified a priori.*		Typically, a clinical protocol will always have to specify the sampling points a priori for study execution. Does the phrase "*should be justified and specified a priori*" imply that Health Canada expects to be consulted on the timepoints? If not, please consider removing the wording to avoid confusion.

REFERENCES

[1] Health Canada. Draft Guidance. 2020 https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/comparative-pharmacokinetic-studies-orally-inhaled-products/document.html .

[2] Notice (Health Canada File number 19-122718-811): https://www.canada.ca/en/health-canada/services/drugs-health-products/public-involvement-consultations/notice-draft-guidance-comparative-pharmacokinetic-studies-orally-inhaled-products.html.